REMARKS

Applicants thank the Examiner for interview of June 26, 2008, during which the foregoing claim amendment strategy was discussed.

Upon entry of this amendment, claims 1-6, 8-15, 17-30, and 43-54, and 56-70 are pending in the application. Claims 16 and 55 are canceled. Claims 1, 5, 6, 8-11, 15, 19, 22-28, 30, 46-50, 54, 58, and 61 are amended. Claims 8-11, 15, 19, 26, 48-50, 54, and 58 are amended to correct typographical errors and for clarity. Support for the amendments to claims 1, 22, and 30 can be found throughout the specification as-filed, *e.g.* at least at page 8, line 26 to page 9, line 2; and at page 16, lines 12-14 of the specification as-filed. New claims 64-70 are added. Support for the new claims can be found throughout the specification, *e.g.*, at least in original claim 1 and at page 16, lines 12-14 of the specification. No new matter is added.

Objections to the Specification

Tables 2 and 3 are objected to for illegible column headings. *See*, Office Action at page 2. The specification is amended so the column headings on Tables 2 and 3 are legible. Reconsideration and withdrawal of this objection is requested.

Rejections under 35 USC § 112, first paragraph

Claims 1-6, 8-21, and 62 are rejected under 35 U.S.C. § 112, first paragraph for lack of enablement. *See*, Office Action at page 2. The Examiner states that according to the specification, GlcNAc (β 1-4) GlcNAc(β) is indicative of anti-phospholipid syndrome. *See*, Office Action at page 3.

> Applicant teaches elevation of antibodies specific for various oligosaccharide structures in patients with inflammatory bowel disease, particularly Crohn's disease. However, detection of elevated levels of anti- GlcNAc (β 1-4) GlcNAc(β) antibodies is specifically taught as indicative of antiphospholipid syndrome (see e.g.: pages 6-7 and 19-20; Fig. 2a). Crohn's disease shares some symptoms with antiphospholipid syndrome, such as anemia. Thus, absent further guidance from applicant, one would not be assured of the ability to successfully practice the invention as instantly claimed because one could not diagnose a patient as having Crohn's disease performing the method as claimed. Moreover, although the headings of Tables 2 and 3 are not clear, it would seem that one could not be assured of the ability to successfully practice the invention of the scope as instantly claimed in the absence of specifically detecting IgA anti-GlcNAc (β 1-4) GlcNAc(β) antibodies in a subject suspected of having Crohn's disease.

In addition to being indicative of anti-phospholipid syndrome, anti-GlcNAc (β 1-4) GlcNAc(β) antibodies were found to be significantly elevated in Crohn's disease as described below (paragraph spanning pages 17-18 of the specification):

> Comparison of the average and median values of anti-carbohydrate antibodies in the CD and other digestive disease populations reveals a significant elevation in most of the anti-glycans antibodies in the CD group as compared to the group containing individuals with the other digestive diseases group. No one of the CD patients was found to be positive for pANCA antibodies. All the anti-glycans levels that are displayed in Tables 2 and 3 show statistically significant (α=0.05; $p<0.05$) differences between the CD groups and the other digestive disease or normal group. Statistically significant differences between the medians of signals of CD and other digestive disease population and normal population were observed for antibodies bound to the following glycans: Glc(β), Glc(β,1-4)Glc(β), Glc(β,1-3)Glc(β), GlcNAc(β) 6-sulfate, Man(α,1-2)Man(α), Man(α,1-3)Man(α), Man(α,1-6)Man(α), Man(α), Man(α,1-3)[Man(α,1-6)]Man(α), Mannan, Dextran, Xylan, GlcNAc(β,1-4)GlcNAc(β), Gal 3-sulphate(β), GlcNAc(β,1-3)GalNAc(β), GlcNAc(β,1-3)Gal(β,1–4)Glc(β), Gal(α), Gal(β) , GalNAc(α), Glc(α) , Gal(β,1-6)Gal(β), GlcNAc(β,1-6)GalNAc(α) and Gal(α,1-3)Gal(β,1-4)GlcNAc(β). (emphasis added)

Thus, the specification and data presented in Table 3 establish that this antibody is elevated in Crohn's Disease. Claim 1, from which claims 2-6, 8-15, 17-21, 62, and 64-66 depend, has been amended to require detecting a level of an anti-GlcNAc (β 1-4) GlcNAc(β) antibody (ACCA) in a sample by binding to a carbohydrate reagent comprising an isolated

GlcNAc (β 1-4) GlcNAc(β) glycan and diagnosing Crohn's Disease by detection of an elevated level of the antibody in the test sample relative to a control sample. Moreover, Applicants have amended claim 1 to require that the anti- GlcNAc (β 1-4) GlcNAc(β) antibody be of the IgA isotype.

Thus, the appropriate inquiry for determining whether the enablement requirement has been satisfied in the present case, is whether the instant specification teaches the ordinary skilled artisan how to diagnose Crohn's Disease by detecting a level of an anti-GlcNAc (β 1-4) GlcNAc(β) antibody (ACCA) in a sample by binding to a carbohydrate reagent comprising an isolated GlcNAc (β 1-4) GlcNAc(β) glycan.

As stated previously, Example 1 illustrates that a statistically significant elevated level of anti-GlcNAc (β 1-4) GlcNAc(β) antibody (ACCA) was detected in the serum of patients with Crohn's Disease as compared to the normal population and individuals with other digestive diseases. *See*, Specification at Example 1, page 17, lines 13-28; and at Table 3, column 3.

For the reasons articulated above, the amount of direction and guidance disclosed in the specification, as well as the general knowledge in the art at the time of the invention, is sufficient to enable the skilled artisan to make and use the claimed methods using only routine experimentation. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1-6, 8-21, and 62 under 35 U.S.C. §112, first paragraph.

Rejections under 35 USC § 112, second paragraph

Claims 1-6, 8-29, 30, and 43-63 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. *See*, Office Action at pages 4-7.

Specifically, the Examiner indicates that in claim 1, it is not clear which or how many symptoms are intended in order to define the subject population. *See*, Office Action at page 4. Claim 1 is amended herein to require providing a test sample from a subject with digestive symptoms of Crohn's disease. Applicants submit that claim 1 is clear and that this rejection should be withdrawn.

The Examiner indicates that in claim 5, the interrelationships of the steps to those of the independent claim and the diagnosis of Crohn's disease are not clear. *See*, Office Action at page 4. Claim 5 requires that the method further comprises detecting a level of at least one of an anti-Glc (β 1-3) Glc (β) antibody and an anti-polysaccharide β-D (1-3) Glucan antibody in the sample. Applicants submit that claim 5 is clear and this rejection should be withdrawn.

The Examiner states that in claim 15, it is not clear which of the antibodies identified is "said" antibody. *See*, Office Action at page 4. Claim 15 is amended herein to require that the method further comprises determining an isotype of said antibody or antibodies. Applicants submit that claim 15 is clear and this rejection should be withdrawn.

According to the Examiner, in claim 6, the interrelationships of the steps to those of the independent claim and the diagnosis of Crohn's disease are not clear. *See*, Office Action at page 4. Claim 6 requires that the method further comprises detecting a level of an anti-Glc (β 1-3) Glc (β) antibody and an anti-polysaccharide β-D (1-3) Glucan antibody in the sample. Applicants submit that claim 6 is clear and this rejection should be withdrawn.

The Examiner states that in claim 8, it is not clear if the diagnosis requires either or both of the antibodies. *See*, Office Action at page 4. Claim 8 is amended to recite that the subject is assessed as having Crohn's disease if the anti-GlcNAc (β 1-4) GlcNAc (β) antibody (ACCA) and

the anti-ASCA antibody are present in the sample. Applicants submit that claim 8 is clear and this rejection should be withdrawn.

According to the Examiner, in claim 9 and 10, it is not clear what diagnosis is to be made if all three of the antibodies are present. *See*, Office Action at pages 4-5. Claims 9 and 10 are amended to recite that the subject is assessed as having Crohn's Disease if the anti-neutrophil cytoplasmic antibodies (ANCA) are absent in said sample, as suggested by the Examiner. Applicants submit that claims 9 and 10 are clear and this rejection should be withdrawn.

The Examiner states that in claim 11, the interrelationships of the steps to those of the independent claim and the diagnosis of Crohn's disease are not clear. *See*, Office Action at page 5. Claim 11 requires that the method further comprises detecting a level of one, two, or three of anti-Man (α 1-3) Man (α) antibody, anti-Man (α 1-3)[Man (α 1-6)] Man (α) antibody, anti-Man (α 1-2) Man (α), anti-Man (α 1-6) Man (α) or an anti-Mannan (ASCA) antibody in the sample. Applicants submit that claim 11 is clear and this rejection should be withdrawn.

The Examiner indicates that claim 19 adds additional anti-glycan antibodies and does not properly limit the previously-recited subject matter. *See*, Office Action at page 5. Claim 19 is amended to require that the method further comprises detecting a level of an anti-Glc (β) IgG antibody, an anti-Glc (β 1-3) Glc (β) IgG antibody, an anti-Glc (β 1-4) Glc (β) IgG antibody, an anti-GlcNAc (β) 6-sulfate IgG antibody, or an anti-Xylan IgG antibody. Applicants submit that claim 19 is clear and this rejection should be withdrawn.

The Examiner contends that in claim 22, it is not clear which or how many symptoms are intended in order to define the subject population. *See*, Office Action at page 5. Claim 22 is amended to require providing a test sample from a subject with digestive symptoms of Crohn's disease. Applicants submit that claim 22 is clear and that this rejection should be withdrawn.

According to the Examiner, in claims 24 and 25, the interrelationships of the steps to those of the independent claim and the diagnosis of Crohn's disease are not clear. *See*, Office Action at page 5. Claim 24 recites that the method further comprises detecting a level of an IgG anti-Man (α 1-3) Man (α) antibody in the sample. Claim 25 recites that the method further comprises detecting a level of an IgG Glc (β 1-3) Glc (β) antibody and an IgG anti-Man (α 1-3) Man (α) antibody in the sample. Applicants submit that claims 24 and 25 are clear and that this rejection should be withdrawn.

The Examiner states that in claim 26, it is not clear if diagnosis requires either or both of the anti-glycan and anti-mannan antibodies. *See*, Office Action at page 5. Claim 26 is amended to require that the method further comprises detecting a level of an IgG anti- Mannan or an IgA anti- Mannan antibody in the sample, wherein the subject is assessed as having Crohn's Disease if the anti-Glc (β 1-3) Glc (β) antibody (ALCA), the IgG anti- Mannan, or IgA anti- Mannan antibody is elevated in the sample. Applicants submit that claim 26 is clear and this rejection should be withdrawn.

The Examiner states that in claim 46, the interrelationships of the steps to those of the independent claim and the diagnosis of Crohn's disease are not clear. *See*, Office Action at page 5. Claim 46 recites that the method further comprises detecting a level of at least one of an anti-GlcNAc (β 1-4) GlcNAc (β) antibody and an anti-polysaccharide β-D (1-3) Glucan antibody in the sample. Applicants submit that claim 26 is clear and this rejection should be withdrawn.

According to the Examiner, in claim 54, it is not clear which of the antibodies identified is "said" antibody. *See*, Office Action at pages 5-6. Claim 54 is amended to recite that the method further comprises determining an isotype of the antibody or antibodies. Applicants submit that claim 54 is clear and this rejection should be withdrawn.

The Examiner contends that in claim 47, the interrelationships of the steps to those of the independent claim and the diagnosis of Crohn's disease are not clear. *See*, Office Action at page 6. Claim 47 requires that the method further comprises detecting a level of an anti-GlcNAc (β 1-4) GlcNAc (β) antibody and an anti-polysaccharide β-D (1-3) Glucan antibody in the sample. Applicants submit that claim 47 is clear and this rejection should be withdrawn.

The Examiner indicates that in claim 48, it is not clear if diagnosis requires either or both of the antibodies. *See*, Office Action at page 6. Claim 48 is amended to require that the method further comprises detecting a level of an anti- Mannan (ASCA) antibody in the sample, wherein the subject is assessed as having Crohn's disease if the anti-Glc (β 1-3) Glc (β) antibody (ALCA) or the anti-ASCA antibody is elevated in the sample. Applicants submit that claim 48 is clear and this rejection should be withdrawn.

The Examiner states that in claim 49 and 50, it is not clear what diagnosis is made if all of the antibodies are present. *See*, Office Action at page 6. Claims 49 and 50 are amended to require that the method further comprises determining whether the test sample has anti-neutrophil cytoplasmic antibodies (ANCA), wherein the subject is assessed as having Crohn's Disease if the anti-neutrophil cytoplasmic antibodies (ANCA) are absent in the sample. Applicants submit that claims 49 and 50 are clear and this rejection should be withdrawn.

The Examiner indicates that claim 58 adds additional anti-glycan antibodies and does not properly limit the previously recited subject matter. *See*, Office Action at page 6. Claim 58 is amended to require that the method further comprises detecting a level of an anti-Glc (β) IgG antibody, an anti-Glc (β 1-3) Glc (β) IgG antibody, an anti-Glc (β 1-4) Glc (β) IgG antibody, an anti-GlcNAc (β) 6-sulfate IgG antibody, or an anti-Xylan IgG antibody in the sample. Applicants submit that claim 58 is clear and this rejection should be withdrawn.

The Examiner contends that claim 61 is unclear as the interrelationships of the steps to those of the independent claim and the diagnosis of Crohn's disease are not clear. *See*, Office Action at page 6. Claim 61 recites that the method comprises detecting a level of the anti- Glc (β 1-3) Glc (β) antibody, and one, two, or three of anti-Man (α 1-3) Man (α) antibody, anti-Man (α 1-3)[Man (α 1-6)] Man (α) antibody, anti-Man (α 1-2) Man (α),anti-Man (α 1-6) Man (α) or an anti- Mannan (ASCA) antibody in the sample. Applicants submit that claim 61 is clear and this rejection should be withdrawn.

The Examiner states that in claim 30, it is not clear which or how many symptoms are intended in order to define the subject population. *See*, Office Action at page 6. Claim 30 is amended herein to require providing a test sample from a subject with digestive symptoms of Crohn's disease. Applicants submit that claim 30 is clear and that this rejection should be withdrawn.

Rejections under 35 USC § 102(b)

Claims 22-28, 43-45, 48, 51-53, and 61 are rejected as anticipated by Main *et al.* BMJ 297:1105, 1988 ("Main") in light of Applicants' disclosure, Sendid *et al.*, Clin. Diagn. Lab. Immunol. 3:219, 1996 ("Sendid"), and/or Wakshull *et al.*, US Patent No. 6,294,321 ("Wakshull"). *See*, Office Action at page 7. Specifically, the Examiner states that the assays of the references inherently detected antibodies to glycan epitopes, *e.g.*, β (1-3) glucans and mannans, present in yeast cells. The Examiner further states that the claims do not require immobilized defined glycans. *See*, Office Action at page 8. Applicants disagree with respect to the claims as amended.

Claim 22, from which claims 23-28, 43-45, 48, 51-53, and 61 depend, has been amended to require detecting a level of an anti-Glc (β 1-3) Glc (β) antibody (ALCA) in the sample by binding to a carbohydrate reagent comprising an isolated Glc (β 1-3) Glc (β) glycan. An "isolated" glycan refers to a purified or chemically synthesized glycan. Neither Main, nor Sendid, nor Wakshull recites detecting a level of an anti-Glc (β 1-3) Glc (β) antibody (ALCA) in the sample by binding to a carbohydrate reagent comprising an isolated Glc (β 1-3) Glc (β) glycan.

Similarly, new claims 67-70 require detecting a level of various anti-glycan antibodies in a sample by binding to a specific glycan on a solid phase. Neither Main, nor Sendid, nor Wakshull recites detecting a level of an anti-glycan antibody in a sample by binding to a specific glycan on a solid phase.

Therefore, Applicants respectfully submit that, contrary to the Examiner's assertions, Main, Sendid, and Wakshull fail to describe or suggest each and every element of the claimed invention expressly and/or inherently and, thus, the references fail to anticipate the claimed invention. For the foregoing reasons, Applicants respectfully request that the rejection for anticipation be reconsidered and withdrawn.

Claims 22-28, 43-45, 48, 51-53, and 61 are rejected as anticipated by Sendid in light of the instant disclosure and/or Wakshull. *See*, Office Action at page 7.

As stated above, neither Sendid nor Wakshull describe or suggest each and every limitation of claim 22, as amended. Specifically, neither Sendid nor Wakshull describe or suggest detecting a level of an anti-Glc (β 1-3) Glc (β) antibody (ALCA) in the sample by binding to a carbohydrate reagent comprising an isolated Glc (β 1-3) Glc (β) glycan, as required by claim 22, as amended.

Similarly, neither Sendid nor Wakshull describe or suggest detecting a level of various anti-glycan antibodies in a sample by binding to a specific glycan on a solid phase, as required by new claim 67, from which new claims 68-70 depend.

Therefore, Applicants respectfully submit that, contrary to the Examiner's assertions, Sendid and Wakshull fail to describe or suggest each and every element of the claimed invention expressly and/or inherently and, thus, the references fail to anticipate the claimed invention. For the foregoing reasons, Applicants respectfully request that the rejection for anticipation be reconsidered and withdrawn.

Claim 30 is rejected as anticipated by Quinton *et al.*, Gut 42:788, 1998 ("Quinton") in light of Walsh et al., US Patent No. 6,218,129 ("Walsh"). *See*, Office Action at page 7.

Claim 30, as amended, requires identifying a specific antibody in a sample by binding to a carbohydrate reagent comprising an isolated glycan. Neither Quinton, nor Walsh recites identifying a specific antibody in a sample by binding to a carbohydrate reagent comprising an isolated glycan.

Similarly, new claims 67-70 require detecting a level of various anti-glycan antibodies in a sample by binding to a specific glycan on a solid phase. Neither Quinton, nor Walsh recites detecting a level of an anti-glycan antibody in a sample by binding to a specific glycan on a solid phase.

Therefore, Applicants respectfully submit that, contrary to the Examiner's assertions, Quinton and Walsh fail to describe or suggest each and every element of the claimed invention expressly and/or inherently and, thus, the references fail to anticipate the claimed invention. For

the foregoing reasons, Applicants respectfully request that the rejection for anticipation be reconsidered and withdrawn.

Double Patenting Rejections

Claims 1-6, 8-30, and 43-63 are provisionally rejected on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 1-7, 9, 11-29, and 73-91 of copending Application No. 10/843,033; claims 29, 55-57, and 59 of copending Application No. 11/351,185; and claims 1-4, 7, 8, 11, 18-22, 28, 30-32, 36, 37, 40, 47-51, 54-65, and 70-73 of copending Application No. 11/364,964. *See*, Office Action at pages 9-10.

Applicants disagree. However, in the interest of expediting prosecution of the present application, Applicants file herewith a terminal disclaimer in compliance with 37 C.F.R. §1.321(c). Withdrawal of this rejection is respectfully requested.

On the basis of the foregoing amendments and remarks, Applicants submit the pending claims are in condition for allowance. Such action is respectfully requested. The Commissioner is authorized to charge any fees that may be due to Deposit Account No. 50-0311, Reference No. 25681-502 P.

Respectfully submitted,

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